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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,005	11/14/2005	Tomoyuki Oomura	TX/4-32997B	6462

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
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EXAMINER	
KASTURI, SRIRAM	
ART UNIT	PAPER NUMBER
4131	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/552,005	OOMURA ET AL.	
	Examiner	Art Unit	
	SRIRAM KASTURI	4131	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/10/2006 & 10/04/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10 are pending. Applicant's two IDS submitted on 11-10-2006 and 10-04-2005 are acknowledged and have been considered.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1, 3-6, and 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kishikawa et al (US 7,151,093 B2).

4. Applicant claims (claims 1, 3-6, 8-10) a solid pharmaceutical composition comprising a S1P receptor agonist, a sugar alcohol (e.g. mannitol) and a lubricant such as magnesium stearate in the form of a tablet or capsule.

5. The teachings of Kishikawa et al (US 7151093 B2) clearly state pharmaceutical application of S1P receptor agonist by oral administration as tablet or capsule (Col 3 lines 27-30 and lines 45-52).

6. Kishikawa et al teachings also state that their pharmaceutical composition may contain a sugar alcohol, such as mannitol, and a lubricant, such as magnesium stearate (Col 3 lines 53-62).

7. The difference between what the applicant is claiming and teachings of Kishikawa et al are that concentrations of S1P receptor agonist, mannitol and magnesium stearate are different. In formulation example 1, sphingosine 1-phosphate (i.e. a S1P receptor agonist) concentration is at 50% w/w and magnesium stearate (lubricant) at 1% w/w, as calculated from total of 10g of all the components. Kishikawa et al also teach oral administration range of 1 mg to 1000 mg (col. 3 lines 28-39) of the active ingredient for an adult human. This range (i.e., 1-1,000 mg) implies that one could vary the amount of active agent present in a solid oral formulation over three orders of magnitude and thus obtain formulations comprising 0.5-5% w/w of S1P receptor agonist (i.e., 1-2 orders of magnitude smaller than the formulation that Kishikawa et al exemplify).

Thus based on teachings of Kishikawa et al it would have been prima facie obvious to an ordinary skilled artisan to obtain formulations comprising (a) S1P receptor agonist, (b) a sugar alcohol and (c) lubricant as set forth above.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kishikawa et al (US 7151093 B2) as applied to claim 1, 3-6, and 8-10 above, and further in view of Kiuchi et al (Synthesis and immunosuppressive activity of 2-substituted 2-aminopropane-1,3-diols and 2-aminoethanols. J. med. chem. 2000, 43, 2946-2961) and Mandala et al (Alteration of lymphocyte trafficking by sphingosine-1-phosphate receptor agonists. Science, 2002, 296, 346-349).

8. Applicant claims (claim 2), compound 1, S1P receptor agonist comprises 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol or a pharmaceutically acceptable salt.

9. Teachings of Kiuchi et al clearly state synthesis of FTY720 which is a hydrochloride salt of 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol. Mandala et al teachings suggest using FTY720 as a S1P receptor agonist.

The difference between Kishikawa et al teachings and applicant's claim 2 is that Kishikawa et al doesn't teach compositions wherein 2-amino-2-[2-(4-octylphenyl)ethyl]propane-1,3-diol (compound1) or a pharmaceutically acceptable salt thereof is the S1P receptor agonist. Whereas teachings of Kiuchi et al and Mandala et al suggest using salt of compound 1, FTY720 as a S1P receptor agonist.

Based on teachings of Kishikawa et al in view of teachings of Kiuchi et al and Mandala et al it would have been obvious for a person of ordinary skill in the art to substitute sphingosine 1-phosphate with FTY720 as the S1P receptor agonist with a reasonable expectation of success, because both FTY720 and sphingosine 1-phosphate are art-recongized S1P receptor agonists.

Thus it would have been prima facie obvious to an ordinary skilled artisan at the time of applicant's invention to obtain formulations comprising S1P receptor agonist per the teachings of Kishikawa et al,Kiuchi et al and Mandala et al as set forth above.

Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kishikawa et al (US 7,151,093 B2) as applied to claim 1 , 3-6 and 8-10 above and further in view of Greven et al (US 4,110,322) and Remington's pharmaceutical sciences, (Ed. Alfonso R. Gennaro, 1990, 18th).

10. Applicant claims the composition of claim1 as described above comprising sugar alcohol (claim 7) 90 to 99.5% by weight of sugar alcohol. Remington's pharmaceutical sciences, indicates mannitol as a preferred diluent. Large quantities of a conventional diluent, like mannitol, is preferred due to its good flow, compressible qualities and low moisture content (col. 2, 2nd para lines 16-18 p1645). In page 1655 under breath freshener tablets mannitol is at 91% w/w, where as active ingredients comprise 2% w/w. The teachings of Greven et al (US 4,110,322) clearly indicate the use of an active ingredient at 0.4% w/w, mannitol at 95% w/w and magnesium stearate at 1% w/w (col.19 lines 44-49). Based on the teachings of Kishikawa et al , Remington's pharmaceutical sciences and Greven et al it would have been obvious for a person of ordinary skill in the art at the time of the instant invention to use the w/w percentage range of active ingredient and sugar alcohol as claimed by the applicant, because it is conventional to use large quantities of diluents (e.g. mannitol) in solid oral dosage formulations wherein a small dosage of active agent is required in said formulations.

Based on these prior art references it would have been obvious for a person of ordinary skill in the art at the time of invention to prepare a solid pharmaceutical composition comprising S1P receptor agonist (0.5 to 5%), mannitol (90-99.5% w/w), and magnesium stearate (1.5 to 2.5%). There would be a reasonable expectation of success upon combination of these prior art teachings, because it is well known in the art to use diluents (e.g. mannitol) and lubricant (e.g. magnesium stearate) in oral dosage form, (e.g. tablet), especially wherein the active agent is present in small amounts.

Conclusion

Claims 1-10 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SRIRAM KASTURI whose telephone number is (571)270-5263. The examiner can normally be reached on Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres or Cecilia Tsang can be reached on 571-272-0867 or 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sriram Kasturi, Ph.D
Examiner

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 4131